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BRIEF REPORT

Brief Report: Gender Identity Differences in Autistic Adults: Associations with Perceptual and Socio-cognitive Profiles

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Abstract
Prior research has shown an elevation in autism traits and diagnoses in individuals seen for gender related consultation and in participants self-identifying as transgender. To investigate this relationship between autism and gender identity from a new angle, we compared the self-reported autism traits and sensory differences between participants with autism who did or did not identify with their assigned sex (i.e. cisgender or trans and non-binary, respectively). We found broad elevation of most cognitive autism traits in the trans and non-binary group (those who identified with a gender other than their assigned gender), and lower visual and auditory hypersensitivity. We contrast these data to existing hypotheses and propose a role for autistic resistance to social conditioning.

Keywords Autism · Gender identity · Transgender · Gender dysphoria · Perception · Bayesian cognition

Introduction

There is increasing interest in the relationship between transgender identities (gender identities incongruent with assigned sex which may result in gender dysphoria and/or require medical gender affirmation), and autism spectrum disorders (referred to collectively here as autism). So far, investigations have recruited samples of gender variant and transgender (often abbreviated to 'trans') individuals through gender identity clinics (Pasterski et al. 2014; de Vries et al. 2010; Skagerberg et al. 2015) or the internet (Kristensen and Broome 2016; Jones et al. 2012).

The earliest studies to find an above-population-average rate of autism characteristics and diagnoses within people with gender dysphoria focused on those seeking medical gender affirmation (Pasterski et al. 2014; de Vries et al. 2010; Skagerberg et al. 2015). Most of these studies' samples were rather small and participants were often responding as part of clinical investigations. These characteristics might reduce the reliability of responses in that population due to fear of being denied treatment (Adams et al. 2017). There is also the possibility that these studies have identified specific important trends in those with the most urgent need for clinical attention related to gender identity. The research on this topic was extended into a broader trans population by gathering a larger sample using the internet and community networks to recruit participants (Kristensen and Broome 2016). Of this sample, 14% had an autism diagnosis versus a population average of 0.62% (Elsabbagh et al. 2012). More recent findings in online samples demonstrated elevated symptoms of depression, anxiety and stress (George and Stokes 2018) in participants with increasing numbers of minority group membership, including those who are both autistic and transgender, making understanding of this phenomenon all the more important. The present study adds another perspective by examining the self-reported autistic profiles of transgender, non-binary and cisgender participants with an autism diagnosis, in an existing database of autistic adults.

Several authors have proposed that autistic traits may in some way cause, or create an illusion of, trans identity. For example, de Vries et al. (2010) suggested as one possibility that rigid thinking could cause misinterpretation of gender-atypical interests, and others have proposed touch-hypersensitivity could lead to clothing preferences that violate gender

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norms (Williams et al. 1996; see also Jones et al. 2012; Jacobs et al. 2014). This interpretation would predict a selective elevation within the trans and non-binary subsample of the proposed mediating autistic trait (i.e. rigid thinking or touch-hypersensitivity respectively). Others have proposed that individuals with autism are more prone to reject ideas they perceive as flawed or logically inconsistent (Kristensen and Broome 2016), such as social conditioning and social norms (Ansara and Hegarty 2011), and this facilitates 'coming out'. This interpretation, by contrast, would predict an (not necessarily selective) elevation of autistic traits associated with social learning.

There is also substantial work investigating the biological basis of both gender identity (especially in trans people) and autism, however there's very limited research on the overlap of both, nor overlapping findings in both groups. One example is congenital adrenal hyperplasia (CAH), a condition in which XX-genotype individuals produce an excess of androgens from their adrenal gland; this gives rise to an elevation in both autism traits (Knickmeyer et al. 2006), and masculine gender expression (as female), but only very slight elevation in non-female identity versus control XX-genotype individuals without CAH (Berenbaum and Bailey 2003). However, research into biological correlates of gender identity (typically focussed on transgender individuals) offers indications that there may be a biological basis for gender identity that is not inherently dependent upon karyotype, genital anatomy or gender of rearing (Swaab 2004).

Neuroanatomical correlates of gender in cisgender participants could be related to either gender or karyotype, or both, and while most of these findings are intermediate in transgender people, many are more assigned-sex congruent, for example brain volume (Hahn et al. 2015) and cortical thickness (Luders et al. 2012; Zubiaurre-Elorza et al. 2013). However, several others are much more congruent with gender identity than assigned sex, most notably volume of and neuron number in the central subdivision of the bed nucleus of the stria terminalis (Zhou et al. 1995; Kruijver et al. 2000). Ramachandran and McGeogh (2007, 2008) found a correlation with gender identity in rates of pre- and postsurgical experiences of phantom genitals, suggesting possible implications for somatosensory cortex functional connectivity.

Direct findings in functional neuroimaging also exist. For example, hypothalamic responses to androstedianone odour are sex-differentiated, an effect which emerges later, and congruent with identity in transgender individuals (Burke et al. 2014). There are also a number of findings that relate resting state functional connectivity to gender identity with potentially interesting findings (Manzouri et al. 2015; Feusner et al. 2017). However, elevated rates of depression, and anxiety (see Dhejne et al. 2016 for review) in this population may distort findings (Yang et al. 2015; Rabany et al. 2017), and screening related to gender identity consultation is unreliable (see above Adams et al. 2017; Edmiston 2018). Therefore this field of work remains inconclusive at present and requires further corroboration.

To relate these physiological findings to the groups of hypotheses we described above, those that propose that autism can cause gender identity differences, or an illusion thereof, would predict qualitative differences in this area between typical and autistic trans people, whereas hypotheses that view autism as a facilitator to 'coming out' would predict only quantitative differences.

To attempt to understand the relationship between gender identity development and autism, we sought to investigate the most likely connections between the differences in perception and cognition associated with autism, and experienced and expressed gender identity. For the purposes of this study, we will refer to AMAB for assigned *male* at birth and AFAB for assigned *female* at birth.

Autism is more commonly diagnosed in AMABs, with ratio estimates between 1.33:1 and 15.7:1 (ADDM CDC 2012) and consensus estimates resting around 4:1 (AMAB:AFAB) (Werling and Geschwind 2013, c.f. Loomes et al. 2017). Therefore, we were interested in gender identities not only in the total sample but also in the AMAB and AFAB subgroups. Likewise, because of the reduced propensity of autistic people to engage in reputation management (e.g. by following social conventions; Cage et al. 2013), and the increasing public awareness and acceptance of the idea that gender does not follow a binary (man/woman) system, we were interested in what proportion of people in our sample identified outside of that binary. The term 'non-binary' refers to individuals whose gender identity is not entirely male/man nor entirely female/woman. Non-binary individuals may reject identification with their assigned sex entirely or to a limited extent, and likewise may partially or entirely embrace or reject identification with terms usually associated with binary genders, such as "man" and "woman". There are few attempts so far to glean a systematic estimate of the prevalence of non-binary identity in the general population, but 3.9% of respondents to a large survey of Dutch adults reported an intermediate, non-binary gender identity (Kuyper and Wijsen 2014).

To further probe the hypotheses discussed above, we compared self-reported autistic traits and sensory sensitivity between the 'cisgender' (assigned-females and assigned-males who identify as women and men, respectively) and 'trans and non-binary' groups. We assessed their traits with the Autism Quotient (AQ-28; Baron-Cohen et al. 2001; Hoekstra et al. 2011), and the Sensory Perception Quotient (SPQ; Tavassoli et al. 2014). These comparisons were then used to shed further light on the relationship between autism and gender identity. We obtained data on rates and correlates of trans and non-binary gender identity in a pre-existing

Table 1 Basic demography of participants organised by gender grouping

	Cisgender[a] men	Cisgender[a] women	Trans[b] AMAB[c]	Trans[b] AFAB[d]
N	297 (44.4%)	272 (40.7%)	25 (3.74%)	75 (11.2%)
Age *M(SD)*	56.9 (14.2)	40.0 (12.9)	48.7 (11.6)	42.9 (9.9)
Employment	46.3%	38.0%	25%	27.8%
Education				
Currently on-going	10.6%	18.2%	16.0%	9.3%
Vocational training	54.0%	52.6%	69.6%	61.8%
Bachelors or higher	21.0%	16.2%	4.3%	11.8%
Living situation				
With parents	50 (16.8%)	44 (16.2%)	5 (20%)	4 (5.33%)
Independent	109 (36.7%)	85 (31.3%)	9 (36%)	24 (32%)
Independent with professional support	31 (10.4%)	34 (12.5%)	6 (24%)	16 (21.3%)
Together with partner and/or children	106 (35.7%)	102 (37.5%)	5 (20%)	20 (26.7%)
Group home	11 (3.70%)	16 (5.88%)	1 (4%)	11 (14.7%)
Other	7 (2.36%)	4 (1.47%)	1 (4%)	2 (2.67%)
Has children?	131 (44.1%)	97 (35.7%)	9 (36%)	31 (41.3%)
Mean (SD) if > 1	2.27 (1.11)	1.97 (0.843)	2.44 (0.831)	1.90 (1.06)

Other than for N, percentages refer to the percentage of the gender group to which the category applies. Participants chose all applicable options for "living situation", so the total of these percentages will exceed 100

Missing data was not included in the statistics given

Percentages differ significantly per group ($p < 0.50$)

[a]Identified gender aligns with assigned sex

[b]Identified gender does not align with assigned sex

[c]Assigned male at birth

[d]Assigned female at birth

sample of autistic people, the Netherlands Autism Register. While the prevalence findings within these data have been reported elsewhere (Dewinter et al. 2017), this paper is the first to study the autistic traits of the cis versus trans autistic individuals, to elucidate possible mechanisms behind the elevated co-occurrence between trans and autistic groups.

Methods

Participants

The sample was recruited via the Netherlands Autism Register (NAR), which is a large database of information provided by autistic individuals and their families and consisted of 669 participants (322 AMABs and 347 AFABs). All participants reported having received a formal diagnosis of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) pervasive developmental disorder or DSM-5 autism spectrum disorder by a qualified clinician unaffiliated to this study. Participants' mean age was 44.67 years (SD = 12.63, range 15.92–80.14). Participants self-reported normal intelligence (IQ > 70) and educational attainment. These and other demographics are given in Table 1.

Measures

In addition to demographic questions including age, education and occupation, participants completed the following:

Autism-Spectrum Quotient; Short. (AQ) (Baron-Cohen et al. 2001; Hoekstra et al. 2011; Chronbach's alpha = 0.86), assesses autism traits with 28 self-report ratings of statements describing autistic traits (or their absence). Five subscales include Attention to detail (α = 0.63/0.68); Social skill (α = 0.76/0.68); Attention switching (α = 0.63/0.62); Communication (α = 0.52/0.49); and Imagination (α = 0.63/0.52).

Sensory Processing Questionnaire. (SPQ) (Tavassoli et al. 2014; Chronbach's alpha = 0.93), assesses sensory hypersensitivity with statements (7 statements per each of 5 sensory domains; psychometrics were not provided for the subscales in the original dataset) about sensory experiences.

Gender Identity This question was a multiple choice between (translated from Dutch); "man", "woman", "somewhat man, somewhat woman", "neither man nor woman", "I don't (yet) know", and "Other" with a free-text entry, which

Table 2 ANCOVAs on autism quotient (age as covariate)

AQ factor	Trans[a]		Cisgender[b]		Difference (trans[a]–cisgender[b])	F(1,611)	p	Partial η^2
	M	SD	M	SD				
Social skills	22.57	3.64	21.48	3.92	1.09	7.634	0.001*	0.014
Switching	13.46	1.85	12.88	2.31	0.58	7.634	0.001**	0.023
Imagination	23.35	4.31	22.75	4.51	0.60	11.468	<0.001**	0.027
Numbers & patterns	13.94	3.59	13.45	3.85	0.49	6.470	0.002**	0.016
Routine	12.16	2.76	12.16	2.41	0.00	1.724	0.179	0.010
AQ total	85.48	11.32	82.73	11.64	2.75	10.179	<0.001**	0.024

*$p < 0.05$, **$p < 0.005$

[a]Identified gender does not align with assigned sex

[b]Identified gender aligns with assigned sex

was then classified according to the content of the write-in. (This follows the two-step method recommended by GenIUSS Group, 2014; Tate et al. 2013.)

Analyses

We first categorized the participants as cisgender, binary-trans (AFABs and AMABs identifying solely as a man or a woman, respectively) and nonbinary-trans (those with identities not encapsulated in "man" or "woman") based on their relative answers to the assigned gender and gender identity questions, and examined the distribution of such identities by assigned sex. Due to a very small number of binary-trans classified participants (N = 6), we merged the binary and non-binary trans groups to form one 'trans and non-binary' sample. 613 provided complete answers to the questionnaires assessed here, and the other 56 were excluded from subsequent analyses.

Our post-hoc analyses examined the differences between cisgender and trans and non-binary participants in AQ and SPQ score with a MANCOVA (covariate; age). To examine whether the role played by sensory differences in the autistic profiles of trans and non-binary autistic participants differed from the cisgender autistic participants, we also performed pairwise comparisons on the bivariate correlation between AQ and SPQ between the four assignation × congruence groups (Fisher r-to-z transformation). To minimise any effect of selection bias we weighted the data to obtain equal groups, and repeated each of the above analyses.

Results

AQ-28 scores in the sample were close to previously published values for self-referred samples with an autism diagnosis ($M = 84.10$, $SD = 11.55$) (Hoekstra et al. 2011). Trans and non-binary participants scored higher than cisgender participants on all AQ factors except Routine (MANCOVA, covarying age: Wilks' lambda = 0.982, $p = 0.045$), a pattern which persists when the data are weighted to account for different proportions of assigned-gender (Wilks' lambda = 0.962, $p < 0.001$) (see Table 2). However, the size of these effects was overall small.

SPQ-Short scores in the sample were close to previously published values for self-referred samples with an autism diagnosis ($M = 43.33$, $SD = 14.73$) (Tavassoli et al. 2014). The trans and non-binary participants scored lower (i.e. less hypersensitive) than cisgender participants on the SPQ (MANCOVA: Wilks' lambda = 0.979, $p = 0.002$ weighted) in the Vision and Hearing subscales only (Table 3), a pattern which again persists when weighted.

The correlation between AQ and SPQ did not statistically differ between cisgender and trans participants (Cisgender; $R = -0.202$, $p < 0.001$. Trans; $R = -0.200$, $p = 0.056$. Fisher's $Z = 0.02$, $p = 0.984$). We performed post-hoc Fisher's tests of all possible combinations of all the gender groups with p-values ranging from 0.718 (AMAB trans versus cisgender males) to 0.960 (AFAB trans versus cisgender males).

We found a high rate of trans and especially non-binary identities in this sample (100 out of 675 participants, 15%). AFAB participants reported such identities (21.6%) more frequently than AMABs (7.8%), $t(673) = 5.14$, $p < 0.001$. Furthermore, just 6% (n = 6) of all trans participants identified as binary (4% (n=?) of trans AFABs identified as binary men, and 12% (n=?) of trans AMABs identified as binary women). This was a significantly higher rate of both trans ($\chi^2 = 125.14$, $p < 0.001$) and non-binary ($\chi^2 = 149.39$, $p < 0.001$) than the Dutch population sample of Kuyper and Wijsen (2014).[1]

[1] Kuyper and Wijsen (2014) used the terms "ambivalent" and "incongruent". We interpret both of these for inclusion in comparison to our trans participants, and "ambivalent" (defined as equal or greater identification with the sex not assigned at birth than the sex assigned at birth) for inclusion in comparison to our nonbinary participants.

Table 3 ANCOVAs on Sensory Processing Questionnaire [Age as covariate; scores re-scaled so that high scores represent greater (hyper-sensitivity)]

SPQ factor	Trans[a]		Cisgender[b]		Difference (trans[a]–cisgender[b])	$F(1,611)$	p	Partial η^2
	M	*SD*	*M*	*SD*				
Smell	14.32	5.80	13.83	5.63	0.49	1.109	0.330	0.001
Vision	6.99	3.00	7.58	3.30	– 0.59	3.929	0.020*	0.016
Taste	4.13	2.11	4.31	2.22	– 0.18	0.966	0.381	0.005
Hearing	7.11	2.98	7.27	3.04	– 0.16	5.625	0.004**	0.012
Touch	10.26	4.23	10.86	4.82	– 0.95	0.614	0.541	0.006
SPQ Total	42.81	13.90	43.86	15.54	– 3.31	0.577	0.562	0.008

*$p < 0.05$, **$p < 0.005$

[a]Identified gender does not align with assigned sex

[b]Identified gender aligns with assigned sex

Discussion

Our results show that trans and non-binary participants scored a little higher on all AQ subscales except routine, and a little lower on the SPQ subscales for vision and hearing. As previously reported (Dewinter et al. 2017), in our sample of autistic adults, trans and non-binary identities are significantly elevated compared to the Dutch population as a whole, and AFAB participants were significantly more likely than AMABs to identify outside the binary female-male categories.

The finding that non-binary identities are most elevated seems to support hypotheses focussed on autistic resistance to social conditioning, which are consistent with existing evidence of the same effect with respect to self-description of sexual orientation (Rudolph et al. 2017). Perhaps elevated rates of trans identity in autism might result from a rejection of the binary cisgenderist norm, which combined with a below-typical concern for social norms could promote the disclosure of the identity. Formulated this way, the reduced impact of the binary cisgenderist norm could be seen as another example of a 'flattened prior' (Pellicano and Burr 2012). Within Bayesian models of cognition (e.g. Sanborn and Chater 2016), past information generates predictions about the likely content of future stimuli as a probability distribution known as a 'prior'. The prior is convolved with a probability distribution of possible interpretations of (sensory) data. The resulting distribution is known as the 'posterior'. The percept is derived directly from the posterior (e.g. the peak). Flattened priors, then, would describe a cognitive system that does not assign as much significance to past knowledge as to present experience. Learned patterns from the past, such as social norms (modelled as a prior) are less significant in autistic people, and therefore attenuate extreme experiences less, resulting in an increased subjective salience (Pellicano and Burr 2012). This seems consistent with the evidence that autistic people are more prone to extreme moods (Mazefsky et al. 2013; Lecavalier 2006) and alexithymia (Gaigg et al. 2016). Extant evidence that automatic imitation is more sensitive to self-similarity in autism (Bird et al. 2007) and that the reward system is preferentially activated by own-gender imitation (Losin et al. 2012) may offer one possible route for this proposed mechanism.

We would therefore propose for future investigation the possibility that the relationship between autism and gender incongruence is better understood as gender incongruence being suppressed in the typically-developing by priors including the social schema of cisgenderism (that is, the assumptions that gender is binary, fixed and defined by genital anatomy). If this hypothesis can be confirmed, it seems probable that the transgender experience of autistic trans people is qualitatively the same as that of typically developing trans people, and that autism is also qualitatively the same in transgender as in cisgender autistic people. Indeed, the very low number of participants identifying exclusively as the sex opposite to their assigned sex is close to earlier estimates of prevalence of transgender identities in the population—perhaps indicating that greater awareness of non-binary identities is a driving force behind recent exponential increases in referrals (Reed et al. 2009; Lyons 2016). One might take this further by suggesting, as our 'Flattened Priors' (Pellicano and Burr 2012)—based interpretation might imply, that being autistic doesn't make people appear trans—being typically developing can make people appear cisgender. A similar effect has been seen with sexual orientation as LGB orientations have become increasingly accepted, rates of LGB identitification have risen (Gallup 2018)

That the rate of trans and non-binary identities is higher in AFABs may suggest that the diagnostic biases in autistic AFABs have distorted our results (by biasing the AFAB part of the sample to have more autistic traits), a difference in the rates of trans and non-binary gender identities by assigned sex between autistic and typically developing populations, which remains to be explained, or a complementary role of experiences of cultural misogyny in facilitating the above described process.

Several hypotheses have been proposed to explain the correlation between autism and trans gender identities. Williams, Allard and Sears (1996) hypothesised that restricted and repetitive interests may lead males with autism to become preoccupied with a range of things which "happen to be predominantly feminine in nature", positioning autistic trans identities as qualitatively different from those of neurotypicals'. Other authors (e.g. de Vries et al. 2010; Jacobs et al. 2014) have discussed the possibility that rigid thinking in autism may lead individuals to misinterpret whatever gender nonconformity they experience, as an indication that they are 'in the wrong gender'. These hypotheses would be compatible with finding a selective elevation of autism traits (Routine and Switching on the AQ, and in the former, Touch Sensitivity on the SPQ) in our trans participants, which we did not find. However, to properly test this hypothesis a rather higher degree of specificity would be needed in the measures to compensate for the heterogeneity of autistic and trans populations. The elevated rates of non-binary identities compared to the typical trans population also undermine these hypotheses. Somewhat conversely, Ansara and Hegarty (2011) suggested that autistic individuals' tendency to direct communication and disinterest in social norms reduces the likelihood that cisgenderism and transphobia will prevent them from disclosing their identities. This hypothesis would predict elevation of the Communication and Social-Skill AQ subscales, which we did find, albeit nonselectively. Kristensen and Broome's (2016) study similarly proposed that autistic individuals' "systematising" approaches to a range of cognitive tasks (Auyeung et al. 2009; Golan and Baron-Cohen 2006; Baron-Cohen 2002) would lead them to regard cisgenderist, binary gender norms as an 'imperfect system', which would also predict that differences more related to cognition and logical thinking—autism traits as measured by the AQ, but not the perception differences on the SPQ—would be elevated in our trans and non-binary subsample. This, too, is consistent with our finding of elevation across the whole AQ except the Routine subscale.[2]

The trans and non-binairy members of our sample reported higher autism characteristics, but lower sensory hypersensitivity. These findings are small and therefore difficult to interpret, but do help better contextualise several existing theories, and lead to the formulation of our priors-based theoretical proposal. They might be further understood within a framework of multiple developmental processes underlying autism differently in different individuals, with the resultant heterogeneity of said population, and therefore the exact mechanisms giving rise to consciously experienced gender incongruence may also differ along the same lines.

[2] Corbett et al. (2009) argue that the desire for routine may be driven by the anxiety that the unpredictability of social environments can cause. Therefore, it seems likely that this is suppressed relative to overall AQ scores in our sample because those individuals with the highest scores may also be those least likely to 'come out' or acknowledge their atypical gender identities.

Limitations

While the unusually high proportion of AFAB participants in this autism sample could be driven by the relative willingness of females to participate in questionnaire-based research, it does raise questions about the equivalence of the AMAB and AFAB portions of the sample. We addressed this by statistically resampling the data; however, there remains some ambiguity about how best to interpret the differing prevalences found here. Future research should use a sample from referrals to autism services.

The AQ-28 and even the SPQ are general measures developed for screening. These might be too general to test for differences between groups pertaining to very specific characteristics. Implicit cognitive-behavioural task measures may be able to probe the 'flattened priors' more directly.

Autisitic individuals sometimes struggle with insight in their own functioning, and this could impact on the ability of some participants to report accurately on these measures, although these effects are most robust in those with co-occurring intellectual disability (Huang et al. 2017), who are not included in the present study.

Autistic trans individuals also experience greater levels of emotional distress that may influence the impact of their symptomatology (George and Stokes 2018). It is therefore possible that the elevated AQ total scores in our trans and non-binary participants were influenced by these effects. However, this would be unlikely to explain the distinct pattern at the subscale level.

Implications for Clinical Practice

Attention to gender identity, and how this is experienced by adolescents and adults with ASD by parents and professionals is advisable, independent from which explanation might hold. Exploring and discussing how autistic adolescents and adults identify their genders might help in offering support, and when needed, gender clinicians should be ready to discuss how to communicate and deal with gender in a cisgenderist, neurotypical world. Therefore, autistic patients of gender clinics, like all patients, will need to know that clinicians will trust in the reliability and authenticity of their descriptions of their gender identities. Autistic people with a gender identity that does not align with their gender assigned at birth may need access to specialized gender teams, who should therefore seek to cultivate expertise in working together with autistic people.

Conclusions

The present results show that trans and especially non-binary identities were elevated in a sample of adults diagnosed with autism, particularly among AFAB participants; and show some differences in their autism traits. Various explanations have been suggested, and remain unsupported. An interesting, and still understudied hypothesis, is the notion that elevated trans or non-binary identities in autism result from an increased likelihood that the identity is recognised and disclosed. We further propose the testable hypothesis that a reduced impact of the cisgenderist binary social norm is an example of a flattened prior, resulting in a greater likelihood of the individual becoming aware of their gender identity.

Author Contributions RW analysed and interpreted the data, supervised by LK and SB, assisted by JD. SB oversaw collection of the data. RW lead the writing of the manuscript with critical feedback from LK, JD and SB at every stage.

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Compliance with Ethical Standards

Conflict of interest Each author declares that s/he has no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research ethics committee and with the 1964 Helsinki declaration and its later amendments.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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